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Event-related potentials elicited during a context-free homograph task in normal versus schizophrenic subjects

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Abstract

Thought disorder in schizophrenia may involve abnormal semantic activation or faulty working memory maintenance. Event-related potentials (ERPs) were recorded while sentences reading “THE NOUN WAS ADJECTIVE/VERB” were presented to 34 schizophrenic and 34 control subjects. Some nouns were homographs with dominant and subordinate meanings. Their sentence ending presented information crucial for interpretation (e.g., The *bank* was [*closed, steep*]). Greatest N400 activity to subordinate homograph-meaning sentence endings in schizophrenia would reflect a semantic bias to strong associates. N400 to all endings would reflect faulty verbal working memory maintenance. Schizophrenic subjects showed N400 activity to all endings, suggesting problems in contextual maintenance independent of content, but slightly greater N400 activity to subordinate endings that correlated with the severity of psychosis. Future research should help determine whether a semantic activation bias in schizophrenia toward strong associates is reflected in ERP activity or whether this effect is overshadowed by faulty verbal working memory maintenance of context.

Keywords

Associates; Homographs; LPC; N400; Schizophrenia; Semantic memory

The sentence “The toast was sincere” may seem absurd on first reading, but is, in fact, a valid sentence. Here “toast” refers to a glass raised ceremoniously, in contrast to a slice of browned bread. This type of word is a homograph and has multiple meanings. For some homographs, meanings may be more or less unusual, depending on their probability of usage in discourse. Homographs are a valuable tool for studies of semantics and language processing because of their unique simultaneous position in multiple unrelated semiotic representations. Consequently, contextual cues must be used to determine which constellation of associates is appropriately accessed in semantic memory. Thus, homographic words have been used by various theorists to test and examine associational principles, notably priming and lexical access (see Simpson, 1984).

One important issue is the time course of contextual effects. If priming, or speeded reaction times, occurred to all associates of a homograph, then it would appear likely that priming operates independently of context, with a serial self-terminating search of the lexicon for the appropriate meaning of a homograph (see Seidenberg, Tanenhaus, Leiman, & Bienkowski,

1982; Stanovich & West, 1983; Swinney, 1979). By contrast, if priming occurs only to the contextually appropriate meaning's associates, then context likely plays a role in preemptively inhibiting the initial spread of semantic activation (see Paul, Kellas, Martin, & Clark, 1992; Schvaneveldt, Meyer, & Becker, 1976; Simpson, 1981).

Onifer and Swinney (1981) concluded that priming in humans had a specific time course: both appropriate and inappropriate homograph meanings were primed immediately after homograph presentation despite initial biasing material, but only the contextually appropriate meanings were primed after 1.5 s. Thus, an intermediate, mixed model of priming may best describe context effects on lexical access. All meanings of homographs are activated upon word recognition, with activation being a function of the relative probability of that particular usage in language. Context-based inhibition of contextually inappropriate meanings appears to activate immediately upon word recognition, with effects at approximately 200 ms after word presentation (see Paul et al., 1992; Simpson, 1984; Tanenhaus, Leiman, & Seidenberg, 1979).

Furthermore, there is some evidence that the initial spread of activation is obligatory and that the context-based inhibition is dependent on conscious perception. Marcel (1980) showed that when words were presented with sufficient time between presentations for context-based inhibition of inappropriate homograph associates to occur, differential context-based priming was observed. However, when the homograph was masked, each of its associates was responded to more quickly (primed) regardless of whether the associate was congruous or incongruous with an initial prime. These results suggest that all associates of a given word are primed upon word perception automatically in semantic memory and that controlled processes in an executive verbal memory system act to inhibit this initial local spread of excitation via global contextual information.

A problem in thinking cohesively, or formal thought disorder, is a cardinal sign of psychosis, and includes such features as a loss of abstraction ability, tangentiality, loose associations, derailment, thought blocking, and overinclusive thinking. The presence of underlying thought disorder is inferred by bizarre or unusual speech in patients, where the "train of thought" follows idiosyncratic paths divorced from preceding material. Chapman, Chapman, and Miller (1964) formalized this aspect of schizophrenic thought disorder as a function of excessive bias to high probability (dominant) meanings of ambiguous words (homographs). Thus, as in the explication of normal cognition, the use of homographs has been useful in examining abnormal cognitive processes in schizophrenia. For example, Rattan and Chapman (1973) designed two multiple-choice homograph tests, one including associated but incorrect choices, the other including only appropriate associates. Schizophrenic subjects performed poorly on the task including incorrect associates, but in the normal range when incorrect associates were absent. Similarly, Roberts and Schuham (1974) reported that schizophrenic subjects' performance dropped directly with increases in associative distractions. Blaney (1974) demonstrated increased bias during lexical access for ambiguous words, and Chapman, Chapman, and Daut (1976) showed that schizophrenic subjects were able to detect weak associates when strong associates were not present. These data together suggest that schizophrenic individuals may have all meanings of homographs established in their lexicon, but are unable to use context to choose subordinate, low probability meanings when those meanings are appropriate, particularly if the contextual cues are temporally remote from the homograph (Cohen & Servan-Schreiber, 1992). The pathophysiology related to this abnormality in schizophrenia is not known.

Two competing mechanisms have been posited to explain the semantic and contextual abnormalities in schizophrenia. One proposed underlying dysfunction is abnormal activation in semantic associative networks. Maher (1983) presented evidence that schizophrenic subjects

show an *increase* in the effect of priming on a lexical decision task. This facilitation of the priming effect has since been replicated by Kwapil, Hegley, Chapman and Chapman (1990) and by Spitzer et al. (1994), who further showed that schizophrenic subjects showed increased second order priming compared with controls (e.g., lemon primes sour, which in turn primes sweet; Spitzer, Braun, Hermle, & Maier, 1993). These data suggest that schizophrenic individuals show greater initial activation in semantic networks than control subjects. This effect may cause an increase in the number of associated concepts and ideas reaching and crowding consciousness, and as such makes a likely candidate for underlying some of the features of thought disorder.

A second possible explanation for schizophrenic thought disorder focuses on the failure of the maintenance and application of context by schizophrenic patients. Here, schizophrenic cognitive abnormalities are due to problems in later executive verbal memory-controlled regulating effects of context on modulating activation in semantic networks, failure to maintain representations in executive verbal memory, and in processing streams of discourse for global meaning (Cohen, Barch, Carter, & Servan-Schreiber, 1999; Schwartz, 1982). For example, with longer intervals between words (stimulus onset asynchronies; SOAs) in priming experiments, schizophrenic subjects appear to perform worse than control subjects (Barch et al., 1996), which suggests that schizophrenia may be characterized by a decay of semantic activation with poor verbal working memory maintenance.

These two models might be reconciled by positing a more intense automatic activation coupled with a deficit in contextual maintenance of verbal working memory traces. This would lead to the most strongly associated semantic concepts being activated longest in verbal working memory, and would explain the bias toward strong associates in schizophrenia described by the Chapmans and colleagues. By contrast, a problem with maintenance and use of context without any initial hyperpriming might predict a problem for contextual integration in schizophrenia to all words regardless of the relatedness between words in sentences or between sentences. Thus, homograph tasks, in which the stimulus is matched for orthography, might help shed light on this debate, because associates can be manipulated for associative strength.

In addition, certain event-related potentials (ERPs) provide measures of brain activity associated with semantic activation and contextual integration. N400 is typically evoked by incongruent (contextually inappropriate) sentence endings (e.g., I take my coffee with cream and *dog*; Kutas & Hillyard 1980, 1982). These endings may be written words or pictures (e.g., Nigam, Hoffman, & Simons, 1992). It is also evoked by single words and is larger to weakly associated as compared to strongly associated subsequent words (Kutas & Hillyard, 1989; Polich, 1985a). N400 appears to be uniquely sensitive to complex information processing of semiotic sequences, and is a viable probe of semantic context and the subsequent priming effects of such context.

In the only ERP study of homograph meaning activation in the literature, Van Petten and Kutas (1987) reported behavioral priming of contextually appropriate homograph meaning associates and N400 to associates of the inappropriate homograph meaning at long SOAs. At short SOAs, there was no differential priming for the meanings (i.e., both homograph meanings were equally primed) and the ERP to nonappropriate associates did not show a clear N400.

N400 is followed by a late positive complex (LPC or P600). LPC appears to be sensitive to the physical characteristics of stimuli (e.g., changes in font size; Kutas & Hillyard, 1980; Polich, 1985a), may also be sensitive to the syntactic arrangement of clauses (Osterhout, Holcomb, & Swinney, 1994), and appears to be larger when memory or categorization tasks are required (Neville, Kutas, Chesney, & Schmidt, 1986; Polich, 1985b), but its functional significance is unknown. LPC may reflect information extraction and analysis after individual

word meanings are activated. In Halgren's (1990) model, the positive component is thought to reflect the context-based inhibition of initial spread of activation and the further analysis of global meaning. LPC is likely composed of two components: a positive event to individual words, and a second positive event to sentence endings reflecting processing of the whole sentence. Importantly, because LPC is typically examined to sentence endings, it may confound the word-based neural activation with the neural processes for integration of the whole meaning of the sentence (see Gunter, Jackson, & Mulder, 1992; Neville, Mills, & Lawson, 1992).

The N400 evoked by words has been little studied in schizophrenia or psychotic disorders. Initial reports using subtraction procedures to isolate N400 (incongruent ending—congruent ending) suggested that N400 was reduced in schizophrenia (e.g., Adams et al., 1993; Grillon, Ameli, & Glazer, 1991). More recent studies, however, indicate that N400 may in fact be increased in schizophrenia, even to congruent sentence endings (hence, subtraction waves tend to cancel all N400 activity; Nestor et al., 1997; Niznikiewicz et al., 1997). Condray, Steinhauer, Cohen, van Kammen, and Kasperek (1999) examined the N400 elicited using a word pair paradigm, and described a lack of greater N400 to unassociated words in schizophrenia patients. However, both patients and controls showed a greater N400 effect to unassociated word pairs when presented in lists containing a high proportion of associated pairs. Nearly all studies have reported a significant delay in N400 in schizophrenia.

LPC tends to be reduced in schizophrenia (e.g., Andrews et al., 1993; Mitchell & Andrews, 1991; Nestor et al., 1997), but few studies have attempted to directly manipulate this component using word-based paradigms. This is particularly important because, as noted by Andrews et al. (1993), the N400 abnormalities reported in schizophrenia may in fact be due to an abnormality of the overlapping LPC.

In the current experiment, ERPs were recorded during a homograph task to obtain physiological measures of brain activity during language processing in schizophrenic and control subjects. Subjects were presented four-word long sentences, some of which contained homographs. The sentence ending on homograph sentences was crucial for selection of homograph meaning, and delivered meaning constraints after all homograph meanings were presumably activated as a function of word usage. If schizophrenia caused a susceptibility to a semantic bias such that dominant meanings were activated, then the responses to sentence endings that affirmed the subordinate homograph meaning should have displayed N400 activity, as the subjects had fallaciously selected the dominant meaning. However, if schizophrenic patients could not maintain activations, then all sentence endings would evoke N400, as the initial priming effects would then have dissipated. By contrast, control subjects were hypothesized to avoid premature meaning selection and to extract the requisite information for interpreting the homograph from the sentence ending. This was predicted to be reflected in greater LPC activity to these endings.

Methods

Subjects

Thirty-four right-handed male schizophrenic patients were recruited from the McLean ($n = 23$) and Brockton VAMC ($n = 11$) inpatient units. All patients were screened for a negative history of electroconvulsive therapy, epilepsy or seizures, head trauma, hearing loss, alcohol dependence or abuse in the last 5 years, and any intravenous drug use. Clinical diagnoses were confirmed with chart review and the Structured Clinical Interview for DSM-III-R (SCID) (Spitzer, Williams, Gibbon, & First, 1990a).

Thirty-four healthy, right-handed men were recruited with newspaper advertisements from the local population. All control subjects were screened for a negative history of drug use,

neurological disease or trauma, and psychopathology (SCID-NP; Spitzer, Williams, Gibbon, & First, 1990b) as well as any family history of psychopathology.

All subjects were native English speakers. All subjects performed the Mini-Mental Status Examination (Folstein, Folstein, & McHugh, 1975) to rule out any dementia or delirium, the information subscale of the Wechsler Adult Intelligence Scale—Revised (WAIS-R; Wechsler, 1981) to test remote memory and fund of information, and the digits forward and backward subscales of the WAIS-R to test immediate/short-term memory.

Subject characteristics and test scores are presented in Table 1. Parents of schizophrenic subjects had a significantly lower social class rating than parents of controls but both groups of parents were essentially middle class (skilled workers, minor professionals) or better, suggesting neither group was underprivileged. Schizophrenic subjects performed slightly worse than controls on the Mini-Mental State Examination, but neither group was delirious nor demented. Patients' fund of information was smaller than controls, with lower WAIS-R information scores, and immediate recall as reflected on the digit span tests of the WAIS-R was poorer.

Sentence Paradigm

Sixty-four sentences were used as stimuli, each four words long. The sentences read "THE *NOUN WAS ADJECTIVE/VERB*," and were separated by an asterisk. The noun was either a homograph or a noun with one meaning. The sentence-ending word (adjective/verb) was always congruent with the noun, and in the case of homographs, constrained its meaning as either dominant or subordinate, based upon probability of usage. Twenty-one homographs were chosen from the word lists established by Chapman et al. (1964) and Wollen, Cox, Coahran, Shea, and Kirby (1980), and selected so that dominant meanings had probabilities of usage approximately three times greater than subordinate meanings. Homographs were presented twice, once with the dominant meaning and once with the subordinate meaning. Usage order was counter-balanced. The homographs and their two sentence endings are presented in Table 2. Twenty-two filler sentences contained nouns with one meaning (e.g., "The cheese was smelly," "The car was new"). Stimuli were presented one at a time according to the rapid serial visual presentation (RSVP) technique on a computer screen for 1 s with a stimulus onset asynchrony of 1.25 s. Subjects sat 1 m from the computer screen. In that schizophrenic subjects are prone to auditory hallucinations and are easily distracted from task, attention was maintained by having subjects read each word out loud softly.

Recording System

Electroencephalographic (EEG) activity was recorded from the scalp through 28 tin electrodes in preconfigured caps (ElectroCap International). Linked earlobes were used as the reference, the forehead as ground. Two electrodes located medially to the right eye, one above and one below, were used to monitor vertical eye movements. Electrodes placed at the outer canthi of the eyes were used to monitor horizontal eye movements. All electrode impedances were below 3 k Ω , and the ears were matched within 1 k Ω . The EEG amplifier bandpass was 0.15 (6 dB/octave roll-off) to 40 Hz (36 dB/octave roll-off). Single trial epochs were digitized at 3.5 ms/sample. Each epoch was of 900 ms duration, including a 100-ms prestimulus baseline. Averaging and artifact rejection were done offline. ERP responses were digitally low-pass filtered at 8.5 Hz with a 24 dB/octave roll-off to remove ambient electrical noise, muscle artifact, and alpha contamination. Within each 320-trial block, epochs from each electrode site were baseline corrected by subtraction of the average prestimulus voltage, and corrected for eye movement artifact using regression-based weighting coefficients when the standard deviations of the corrections were <0.01 μ V (Semlitsch, Anderer, Schuster, & Presslich, 1986). Subsequently, epochs which contained voltage exceeding ± 75 μ V at F7, F8, Fp1, or

Fp2 were rejected. Homographic nouns (position 1) were separated as a function of whether the subsequent sentence ending affirmed the dominant, high probability of usage meaning ("ambiguous-high" noun) or the subordinate, low probability of usage meaning ("ambiguous-low" noun). Sentence endings for homograph sentences either affirmed the dominant homograph meaning (ambiguous-high ending) or affirmed the subordinate meaning of the homograph (ambiguous-low ending). Averages were computed separately for each of these two noun and sentence-ending word types.

Analyses

Groups were compared on the amplitudes and peak latencies of N400 and LPC. N400 amplitude for each site was measured as the average voltage over a 50-ms interval centered about the largest negative peak at Cz from 300 to 800 ms. LPC amplitude for each site was measured as the average voltage over a 50-ms interval centered about the largest positive peak at Cz following N400. The peak latencies at Cz for N400 and LPC were used for latency analyses. Repeated-measures analysis of variance (ANOVA) was used to assess differences in N400 and LPC. Diagnostic group was the between-subjects factor (schizophrenia vs. control). Word position (noun vs. sentence ending) and word type (dominant homograph meaning (ambiguous-high) and subordinate homograph meaning (ambiguous-low) were within-subject factors. Effects were assessed separately along the traditional midline (Fz, Cz, Pz) and at lateral temporoparietal sites corresponding to Wernicke's-right and -left (TCP1 and TCP2). The Huynh-Feldt epsilon was used to correct *df* for the sagittal midline site factor (three levels).

Results

Grand-averaged ERP responses to nouns and sentence endings for each group at Fz, Cz, Pz, and lateral temporoparietal sites are presented in Figure 1. The primary effect on this task in control subjects was a broad increase in positivity ranging from roughly 300 to 600 ms in the responses to the sentence endings relative to nouns. This increase was lacking in schizophrenic subjects. By contrast, the ERPs to nouns were more similar between groups, with a more restricted frontocentral LPC reduction in the schizophrenic subjects.

Mean group amplitudes of N400 and LPC to nouns and sentence endings in each group are presented in Figure 2 for the midline sites. Along the midline, N400 amplitude showed a trend for differences between groups, $F(1,66) = 3.36, p = .07$. This apparently smaller N400 in controls was largely due to differential activation of N400 to sentence endings. N400 amplitude was more positive to sentence endings than to nouns, $F(1,66) = 6.53, p = .01$. Of primary importance was a group by position interaction, $F(1,66) = 12.09, p < .01$, that revealed this position effect to be largely due to a reduction of N400 amplitude to sentence endings in the control subjects, $F(1,33) = 20.61, p < .01$, but not schizophrenic subjects, $F(1,33) = 0.38, p = .54$. There were no significant differences in N400 along the midline for the different word types, nor any interaction between word type and group. N400 amplitude was not significantly different among the different midline sites.

N400 latency at the vertex was prolonged in schizophrenic subjects, Controls: 435.5 ms, Schizophrenia: 497.5 ms, $F(1,66) = 16.35, p < .01$. N400 latencies were later for sentence endings relative to nouns in both groups, Controls: 427.4 and 443.7 ms, Schizophrenia: 489.8 and 505.3 ms for nouns and sentence endings, respectively, $F(1,66) = 4.0, p = .05$.

Midline LPC amplitude was larger in controls than in schizophrenics, $F(1,66) = 4.05, p < .05$. There was a trend for LPC to be larger to sentence endings than to nouns, $F(1,66) = 2.83, p < .1$, showing moderate increase to sentence endings in both groups. LPC amplitude was unaffected by word type, with no interactions between word position or group. LPC was larger

frontally than posteriorly in both groups, $F(2,132) = 11.67, p < .01, \epsilon = 0.67$. LPC latency was shorter in controls, Controls: 558.6 ms, Schizophrenia: 613.2 ms, $F(1,66) = 16.35, p < .01$.

N400 and LPC amplitude from the temporoparietal sites are presented in Figure 3. N400 amplitude was smaller to sentence endings than to nouns, $F(1,66) = 4.86, p = .03$. Like for midline sites, there was a group by position interaction, $F(1,66) = 5.03, p < .03$. This effect was largely due to decreased N400 to sentence endings in controls, $F(1,33) = 19.19, p < .01$, but not in patients, $F(1,33) < 0.01, p > .98$. Although N400 was not significantly asymmetrical, there was an interaction between laterality and group, $F(1,66) = 5.18, p < .03$. Schizophrenic subjects showed an N400 more negative on the right, but voltage in the controls was, in general, more negative on the left.

LPC at lateral sites showed a trend for reduction in the schizophrenic group, $F(1,66) = 3.42, p < .07$. LPC was larger to sentence endings than to nouns in both groups, $F(1,66) = 4.9, p = .03$. There was no significant lateral distribution, and although groups appeared to show a reversed asymmetry, the group by side interaction was not significant, $F(1,66) = 2.28, p < .14$.

Spearman's rank-order correlations were performed between Mini-Mental Status Examination and WAIS-R Information scores, and N400 amplitude to sentence endings in the schizophrenic group to assess whether the differences in N400 between groups to sentence endings might be attributed to a general cognitive deficit in the schizophrenia group, given their lower scores on these cognitive measures. There were no significant correlations between N400 to either sentence-ending type and Mini-Mental scores at Fz, Cz, or Pz. There was a general negative association between WAIS-R Information and N400 amplitudes, attaining significance only for N400 to ambiguous-high endings at Pz, $r = -.38, p = .03$. This suggests that more abnormal N400 activity to sentence endings was related to a greater fund of information. Medication dosage was correlated with N400 to ambiguous-high sentence endings only at Cz, $r = .37, p < .04$. N400 to ambiguous-low sentence endings was not correlated significantly with either Mini-Mental scores, WAIS-R Information scores, or medication dosage. By contrast, N400 amplitude elicited by ambiguous-low, but not by ambiguous-high, sentence endings was negatively correlated with the thinking disturbance factor of the Brief Psychiatric Rating Scale (Overall & Gorman, 1962) at each midline electrode site, Fz: $r = -.38, p < .03$; Cz: $r = -.34, p < .05$; Pz: $r = -.42, p < .02$. These results suggest that the greater the degree of thinking disturbance in the psychotic individual, the more negative the N400 elicited by sentence endings that affirm the subordinate homograph meaning.

Discussion

Control subjects demonstrated a decrease in N400 amplitude to all sentence endings relative to nouns, but schizophrenic subjects did not. Schizophrenic subjects also showed a lack of LPC activity to all words, although both groups showed a moderate increase in LPC for sentence endings relative to nouns. The presence of greater N400 to sentence endings in the schizophrenic patients suggests an abnormality that is independent of the content of the sentence, arguing more for a generalized processing dysfunction, for example, a failure of contextual information maintenance (Cohen et al., 1999).

A processing bias dependent on the content of the sentences was predicted to cause greatest N400 amplitude in schizophrenic patients to sentence endings that affirmed the subordinate homograph meaning. The differential patterns of ERP activity to sentence endings indicated that the schizophrenic subjects showed greatest N400 activity to ambiguous-low meanings. The N400 elicited on ambiguous-low sentences showed a correlation with the degree of thinking disturbance. These data are suggestive of incongruity of ambiguous-low sentence endings, which by nature of the paradigm design must necessarily be provided by the subject,

and appear to be proportional to the severity of thought problems in the patient. This theory is in line with the idea that schizophrenic subjects are selecting high-probability meanings of homographs upon presentation as a function of associate strength (Chapman et al., 1964). However, this pattern lacks statistical support, and thus remains speculative.

This N400 reduction to sentence endings in controls may reflect an underlying early positive event. The waveforms in controls to the sentence endings show a broad positive increase relative to nouns that overlap with N400. In schizophrenic subjects N400 to sentence endings was below baseline and more negative on the right, but in controls N400 was above baseline and more positive on the right. The lateral distribution in controls is more typical of LPC (Kutas & Hillyard, 1982). Although LPC amplitude was smaller to all words in schizophrenic subjects than in controls, patients, like controls, showed a moderate midline and a significant lateral increase in LPC to sentence endings. Because the late LPC to sentence endings is thought to reflect the analysis of global sentence meaning (e.g., Neville et al., 1992), global sentence meaning is likely being processed at least to some degree in patients. Together these data suggest that the lack of reduced N400 activity in schizophrenic patients to sentence endings reflects the lack of an early positive event that significantly overlaps with N400. This positive event is likely the early word-based LPC (Gunter et al., 1992; Neville et al., 1992). The present data, though, are unable to definitively answer whether the ERP differences between groups to sentence endings reflect a differential N400 effect, a differential LPC effect, or some combination thereof.

The relation between this lack of positive activity to sentence endings in the schizophrenic group and the P300 on auditory target selection tasks is unclear. Auditory P300 amplitude to low-probability targets (oddballs) has been reported by many laboratories to be abnormal in schizophrenic subjects (e.g., Ford et al., 1994; Salisbury, Shenton, & McCarley, 1999). On such tasks, the P300 also tends to show a left-sided reduction in schizophrenia (Morstyn, Duffy, & McCarley, 1983; Salisbury et al., 1999). In this language task, the sentence ending contains the information necessary to determine the appropriate homograph meaning. When the information selects the subordinate meaning, the stimuli may be considered isometric with the oddball; a stimulus that provides information about the presence of a low-probability event. Thus the broadly reduced LPC and the failure to generate an early LPC to sentence endings may be related to the robust failure to generate P300 in simple target detection tasks. However, the LPC to sentence endings generally is larger on the right than the left, and thus has a different lateral distribution than the oddball P300. The LPC likely arises from different brain generators, rather than a different relative activation of similar sources as is caused by manipulation of parameters in an auditory task, and is evoked during much more complex cognitive operations. It remains most parsimonious then, to suggest that although the LPC and the oddball elicited P300 may reflect “cognitive closure” at some abstract level, the oddball-elicited P300 may be substantially different both at a physiologic and psychological level from the LPC evoked on this language task, and direct comparison of the potentials is premature.

Schizophrenic patients showed slowed activation for both N400 and LPC relative to controls. This observation likely reflects slowed processing regardless of the sentence content in semantic and verbal working memory systems in the schizophrenic patients. The fact that N400 was longer in latency to sentence endings in both groups suggest that language-processing operations were acting similarly, despite the apparently slowed semantic activation in the patients.

Interpretation of the results of this experiment is clouded by several aspects of the protocol. On a passive reading task groups may be reading the sentences at different depths. Connolly, Stewart, and Phillips (1990) and Bentin, Kutas, and Hillyard (1993) have suggested that N400 on a passive reading or phonological task is analogous to the N400 elicited on tasks requiring

semantic processing, suggesting that N400 is an obligatory response when attention is directed to any degree to language stimuli. Although N400 has been evoked in passive reading tasks in normal subjects, it may be increasingly elicited during active reading. Nonetheless, N400 appears to be activated and within the normal range in schizophrenia on passive tasks (e.g., Andrews et al., 1993), and thus the abnormality present in long latency positive activity in schizophrenia in this study is the more striking. For the present protocol, however, there is no direct knowledge of the actual processing of the subjects. Currently, the subjective judgement of meaningfulness of the sentences during ERP acquisition and the effect of this subjective interpretation are being assessed on a new sample of schizophrenic patients to determine whether there is an automatically driven processing bias in schizophrenia toward strong associates, behaviorally thorough error rates and electrophysiologically through separation of correctly interpreted and misinterpreted sentences. The use of vocalization by subjects to monitor behavior on-task may lead to the inclusion of time-locked motor potentials in the averages. This strategy is not unheard of in the schizophrenia literature, as these subjects are prone to attentional lapses. Using responses after completion of each sentence as a metric of attention may well serve to monitor performance without the potential pitfall of time-locked artifact. However, it seems reasonable to assume that within-group latencies of any articulation artifact should be similar to all words, and thus any within-group effects are likely not differentially affected by this potential artifact. In addition, the generalizability of these results to female schizophrenic patients is unclear, as only right-handed male subjects were tested. This skewed subject pool in large part reflects the hospitalized population, as men are far more likely to require hospitalization than women, and have a longer and more severe course of schizophrenia. The inclusion of right handers only assures that lateralization of function is similar for subjects.

The results of this experiment revealed a lack of an N400 positional effect to disambiguating sentence endings, and a lack of late LPC to all words in the schizophrenic subjects on homographic sentences. This effect may be explained by a general problem in maintenance of verbal working memory context (Cohen et al., 1999). However, the differential pattern of ERPs to sentence endings was weakly suggestive of a processing bias in schizophrenia toward strong associates. The sensitivity of ERPs, a measure of brain activity, to this aberrant activation pattern may provide an objective metric of the cognitive dysfunction underlying thought disorder, a major component of schizophrenic psychopathology, as the N400 to subordinate homograph meaning-affirming sentence endings was correlated with the severity of thinking disturbance. However, further research, with more precise control of depth of processing and objective measures of subjective interpretation, is necessary to assess the sensitivity of ERPs to this hypothetical bias or whether faulty verbal memory maintenance and faulty relational analysis of propositions lead to ERP abnormalities on all sentences in schizophrenia regardless of the probability of any specific word's meaning.

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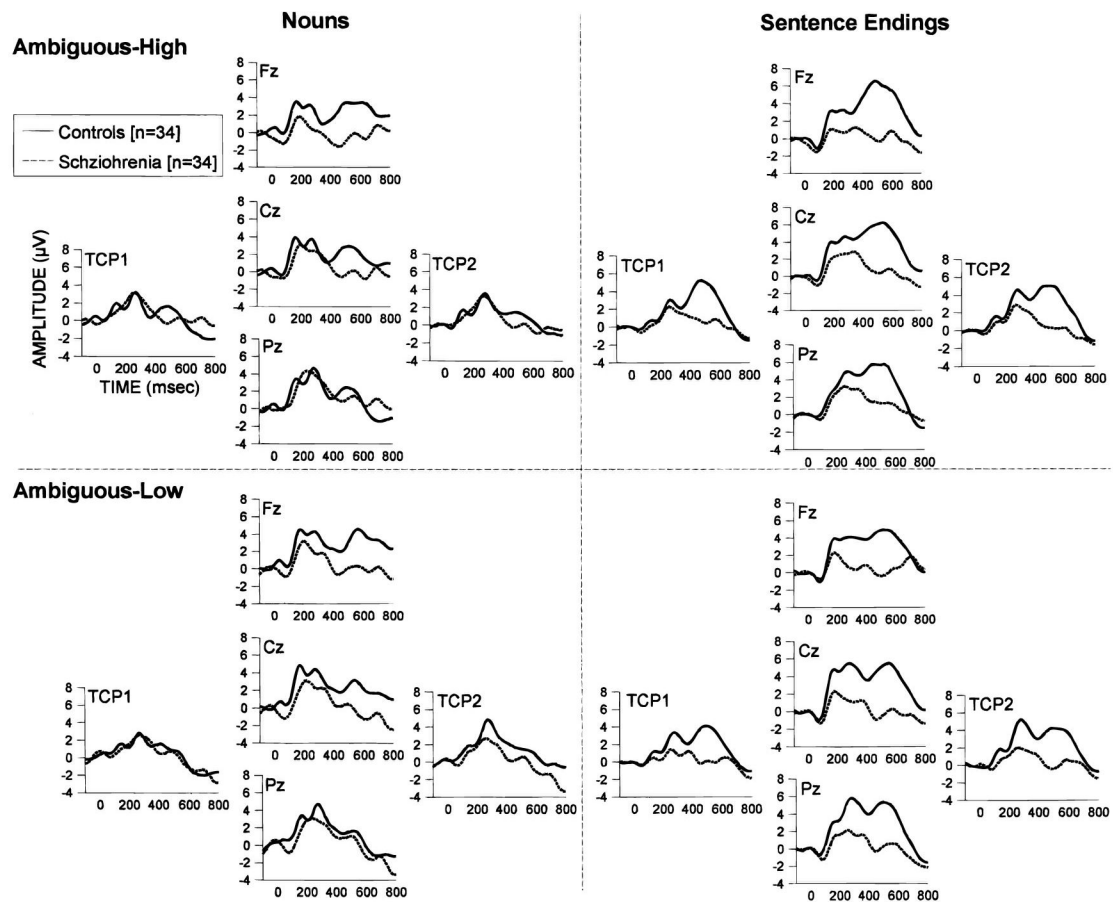


Figure 1.

Grand-averaged waveforms from each group at sagittal midline (Fz, Cz, Pz) and lateral (TCP1 and TCP2) electrode sites. Event-related potentials (ERPs) are presented for nouns (sentence position 2) and sentence endings (sentence position 4). *Note:* Ambiguous-high: Homograph sentences in which the dominant, or high-probability, homograph meaning is affirmed by the sentence ending. Ambiguous-low: Homograph sentences in which the subordinate, or low-probability, homograph meaning is affirmed by the sentence ending.

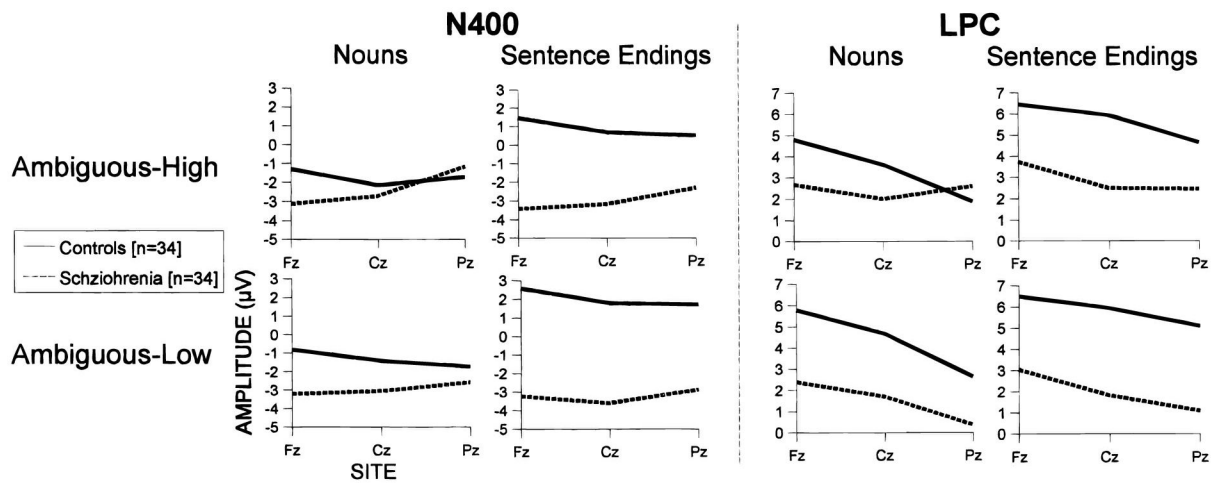


Figure 2. Group mean integrated amplitudes of N400 and LPC along the midline to nouns and sentence endings.

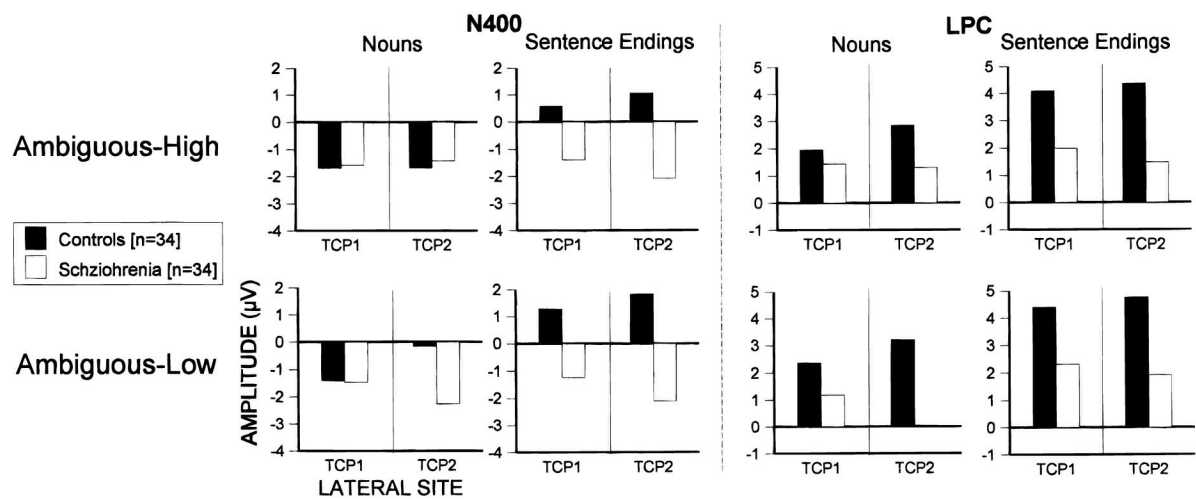


Figure 3. Group mean integrated amplitudes of N400 and LPC at lateral temporoparietal sites to nouns and sentence endings.

Table 1
Basic Demographic, Cognitive, and Clinical Measures

| | Controls | Schizophrenics | <i>p</i> |
|---------------------------------|------------|----------------|-----------|
| Age | 35.6 ± 8.7 | 38.1 ± 6.7 | <i>ns</i> |
| Handedness ^a | 0.80 ± 0.2 | 0.78 ± 0.2 | <i>ns</i> |
| SES ^b | 2.2 ± 1.1 | 4.3 ± 0.9 | <.01 |
| Parental SES | 1.9 ± 1.0 | 2.7 ± 1.1 | <.01 |
| Mini-Mental ^c | 29.2 ± 1.6 | 26.9 ± 3.1 | <.01 |
| WAIS-R Information ^d | 21.7 ± 7.0 | 14.7 ± 6.3 | <.01 |
| WAIS-R Digits-forward | 8.6 ± 2.2 | 5.9 ± 1.9 | <.01 |
| WAIS-R Digits-backward | 7.6 ± 2.5 | 4.4 ± 2.0 | <.01 |
| GAS ^e | | 33.6 ± 14.8 | |
| BPRS ^f | | 38.3 ± 9.5 | |
| Medication ^g | | 381.6 ± 39 | |

Note: Values are mean ± SD.

^aOldfield (1971). -1 = left-handed, 1 = right-handed.

^bSocioeconomic status, Hollingshead (1965). 5 = lowest, 1 = highest.

^cSummed scores Mini-Mental Status Examination (range 0–30), Folstein et al. (1975).

^dSummed raw scores Wechsler Adult Intelligence Scales, Wechsler (1981).

^eGlobal Assessment Scale, Endicott et al. (1976).

^fBrief Psychiatric Rating Scale, Overall & Gorman (1962).

^gChlorpromazine equivalents.

Table 2

Homographs and Sentence Endings

| Homographs | Dominant sentence endings | Subordinate sentence endings |
|------------|---------------------------|------------------------------|
| Corn | Tasty | Aching |
| Suit | Silk | Pending |
| Bank | Closed | Steep |
| Straw | Growing | Clogged |
| Pen | Blue | Fenced |
| Organ | Transplanted | Played |
| Log | Pine | Typed |
| Ruler | Wooden | Mean |
| Interest | Fading | Cheap |
| Plot | Complex | Square |
| Barrel | Leaky | Rifled |
| Toast | Burnt | Sincere |
| Page | Torn | Hairy |
| Pit | Deep | Bitter |
| Plane | Flying | Sharp |
| Date | Fun | Chewy |
| Crack | Jagged | Personal |
| Note | Signed | Off-Key |
| Grain | Planted | Knotty |
| Lock | Metal | Blonde |
| Seal | Furry | Open |